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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/782,750	02/19/2004	Joseph P. Vacanti	MIT 6917 (CMCC 450) DIV	5014

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EXAMINER	
ISABELLA, DAVID J	

ART UNIT	PAPER NUMBER
3738	

DATE MAILED: 03/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/782,750	Applicant(s) VACANTI ET AL.	
	Examiner DAVID J. ISABELLA	Art Unit 3738	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 13 March 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See attached Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

DAVID J ISABELLA
Primary Examiner
Art Unit: 3738

Electton/Restrlcïlons

Applicant's agues that there can be no use of the cell matrix other than with the claimed method. The language of "for use as a heart valve or heart valve leaflet:" does not exclude the construct to be used in other methods. The language is and intended use but does not exclude or prohibit the construct to be used for other applications. The claim as worded is broadly directed to a cell-matrix construct comprising a fibrous polymeric matrix having a shape; the matirxi is formed of biodegradable polymer having seeded cells thereon. Moreover, the construct requires the myofibroblasts be cultured to confluence and then endothelial cells are seeded on the confluent matrix. The method does not require the respective steps for seeding the cells and the method for making the construct must take place in vivo whereas the construct of claims 16 and 17 do not have such requirement. As outlined in the last Office action, the newly submitted claims 16 and 17 are directed to an invention that is independent or distinct from the invention originally claimed because the newly added claims are directed to a "cell matrix construct" seeded with myofibroblasts. The original claims were directed to a method for making a cell matrix construct including implanting a construct into an animal. The construct of claims 16-17 does not require it to be specific to vivo harvesting and therefor is directed to subject matter not originally considered.

Rejection under 35 USC 103

Applicant argues that the prior art must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure.

Applicant attempt to remove Sparks as a base reference is not convincing. Applicant argues that the implant of Sparks includes structures such as an outer die member, inner die member screws, ring and no way can these metal structures be compared to a fibrous mesh. Applicant further argues that the claim requires the construct be formed entirely of a mesh. Examiner respectfully disagrees with applicant's interpretation of Sparks and Claim 1. With respect to Sparks, Dacron mesh is utilized as the fabric (ie. fibrous matrix) upon which cells are seeded. The various metal structures are utilized as support or framework to support mesh in the proper configuration. With respect to the requirement that the construct be fromed entirely of a mesh, examiner contends that claim 1, as broadly worded, does not preclude the use of additional structure, including supporting or framework for supporting the fibrous matrix. In keeping with proper analogy between the claimed invention and the construct of Sparks, one with ordinary skill in the art would equate the fibrous matrix of the claim to be equivalent in structure and function to the Dacron mesh of Sparks.

As argued by the examiner, Sparks clearly discloses a method for making a cell-matrix construct for use as a heart valve comprising implanting into an animal a fibrous

matrix formed of a polymer that has been seeded with specific selected cells. Contrary to applicant's arguments that Sparks fails to disclose a method for making a shaped construct in the likeness of a heart valve, examiner directs applicant's attention to column 5, lines 5-75. In column 5, Sparks specifically discloses the method for forming any of a tricuspid, bicuspid or individual valve leaflets. Clearly, the resulting construct of Sparks is in the form of a heart valve as broadly claimed by applicant. . It should be evident that at the time of Sparks invention (1967) the use of resorbable material in tissue applications was in its infancy. At the time of applicant's invention (2004), great strides have been made in the prosthetic art in replacing non-resorbable materials with resorbable materials for various known benefits. The use of resorbable material as the substrate for seeding cells to form a tissue construct would have been obvious to one with ordinary skill in the art from the teachings of any of the secondary references. Examiner argued that Applicant specification is silent any unobvious benefits in the selection of the materials used for the seeding of the cells. Accordingly, examiner maintains that the materials used by applicant are well known in the art and are in many instances, known equivalents as taught by Jauregui or Tang et al. Specifically, Tang, et al teaches that bioabsorbable material play critical role in fabrication of devices used for tissue regeneration.

> Bioresorbable polymers have been used in the fabrication of devices for implantation in living tissue for several decades. Medical application of such polymers include absorbable sutures, haemostatic aids and, recently, intraosseous implants and control-release drug delivery systems, to name but a few. Use of such polymers has been extended to tissue regeneration devices such as nerve channels, vascular grafts, sperm duct channels, fallopian tube ducts or channels and the like. To be effective, these devices must be made from materials that meet a wide range of biological, physical and chemical prerequisites. The material must be bioresorbable at least in part, nontoxic, noncarcinogenic, nonantigenic, and must demonstrate favorable mechanical properties such as flexibility, suturability in some cases, and amenability to custom fabrication.

Moreover, Tang et al teaches essential equivalent nature between Dacron and bioresorbable material in heart valve applications.

> The rate of bioresorption and/or biodegradation exhibited by the device of this invention will vary depending on the desired longevity of the device. For example, because of the relatively high degree of compatibility between the biopolymers used in the construction of the device of this invention and blood and tissue of living systems, one device of this invention is a conventional part which contacts blood or living tissue such as tubing of an extracorporeal loop or other types of flow-through systems for blood, heart valves and the like. In such instances, the device should be formed or at least have a surface which will contact the blood and/or the living tissue coated with a biopolymer having a relatively slow rate of bioresorbability and/or biodegradeability or which is even relatively biodureble. On the other hand, another device of this invention is a vascular graft composed of a fabric composed of a relatively biodurable material such as Dacron or a bioresorbable biopolymer having a relatively slow rate of bioresorption coated with a relatively fast bioresorbing biopolymer, especially in the inside of the graft. The use of the coating having fast rate of bioresorption provides for a regenerated blood vessel having a high degree of patency and relatively low rate of thrombosis.

Schmidt, et al , Griffith-Cima.and Mikos biodegradable matrix are designed to allow biological tissue ingrowth to form a structure before the matrix is completely bioabsorbed. To replace the non-absorbable mesh of Sparks with an absorbable matrix as taught by Schmidt, et al, Mikos or Griffith-Cima. to allow for a

degradable template for new tissue formation would have been obvious to one with ordinary skill in the art.

With respect to the limitation of "withstand repeated stress and strain", the device of Sparks as modified would inherently possess the propertes that would be capable of withstanding cyclic stresses and strains since the valve is designed to function as a replacement of a natural existing valve.

David J. Isabella
Primary Examiner